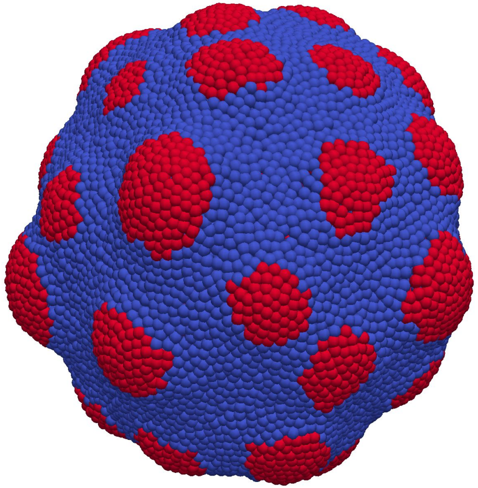
Equilibrium Shape Fluctuations Of Heterogeneous Biological Membranes

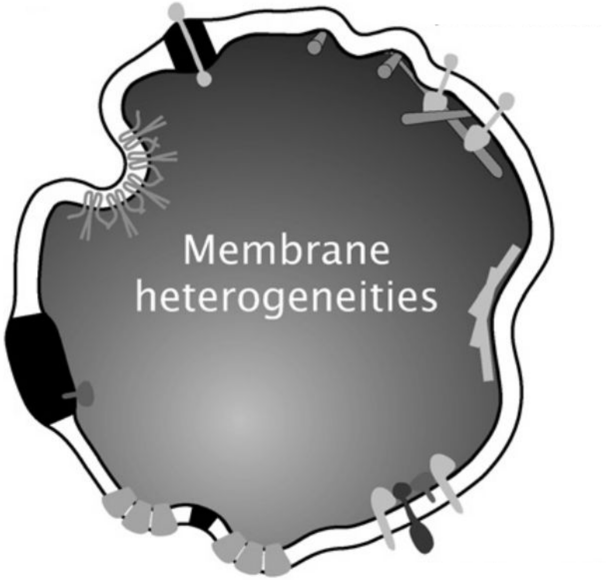
David Rower
advised by Paul Atzberger



Outline

1) Background: experiment and theory
2) Single Bead Model
3) Bending rigidity estimation
4) Toy discussion of adhesion
5) Future work

Biological Membranes: Motivation



from *Soft Matter*, 2009, 5, 3174–3186

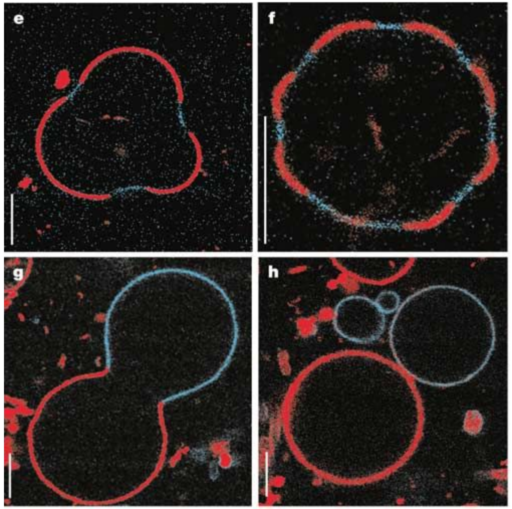
Relevance

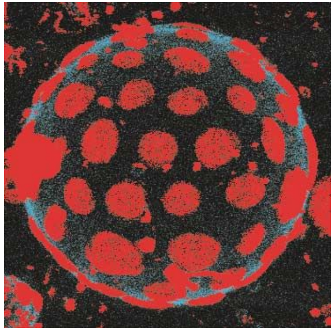
- Endo/exocytosis
- Cell division
- Autophagy
- Tubulation

Biological Membranes: Brief Background

Recent Experiment

Fluorescent Imaging: Baumgart et al. (2003)





Biological Membranes: Brief Background

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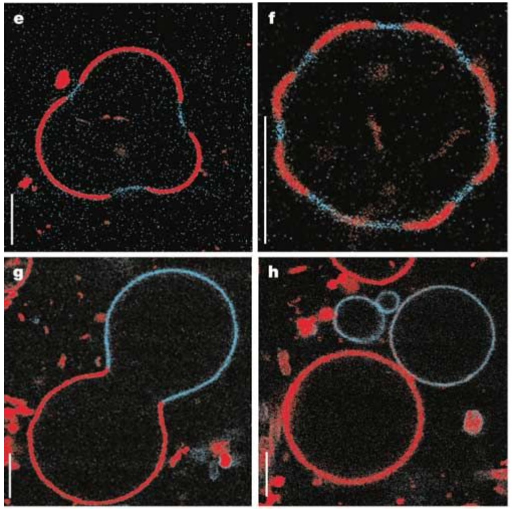

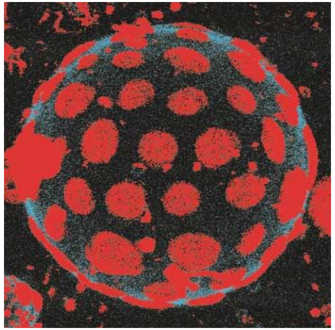

Recent Simulation

Membrane stiffness decreases with concentration of integral membrane proteins: Fowler et al. (2016)

Biological Membranes: Brief Background

Recent Experiment

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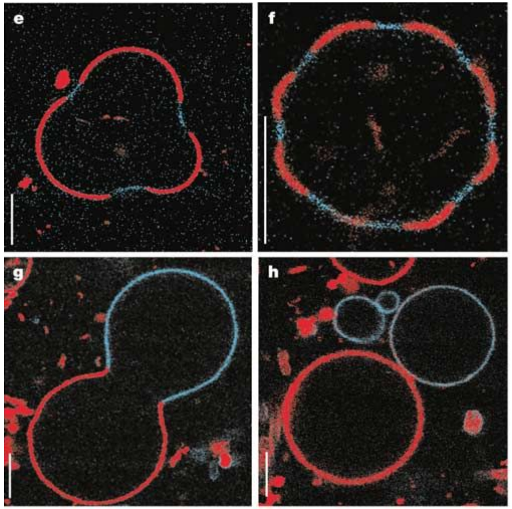
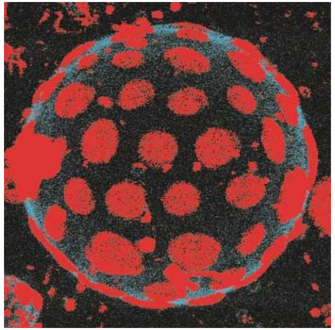




Recent Simulation

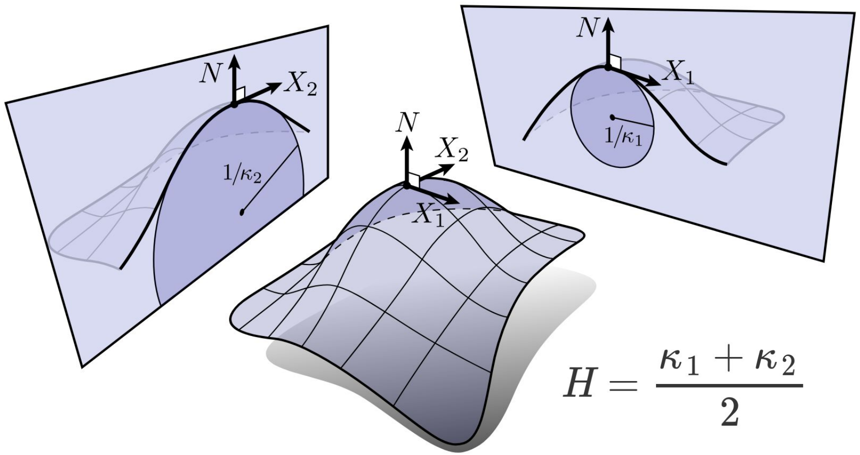
Membrane stiffness decreases with concentration of integral membrane proteins: Fowler et al. (2016)

“...bending stiffness decreased monotonously with increasing curvature ...”: Tian et al. (2009)
(in context of tubular membranes)

Biological Membranes: Brief Background

Theory

Differential Geometry (Curvature)

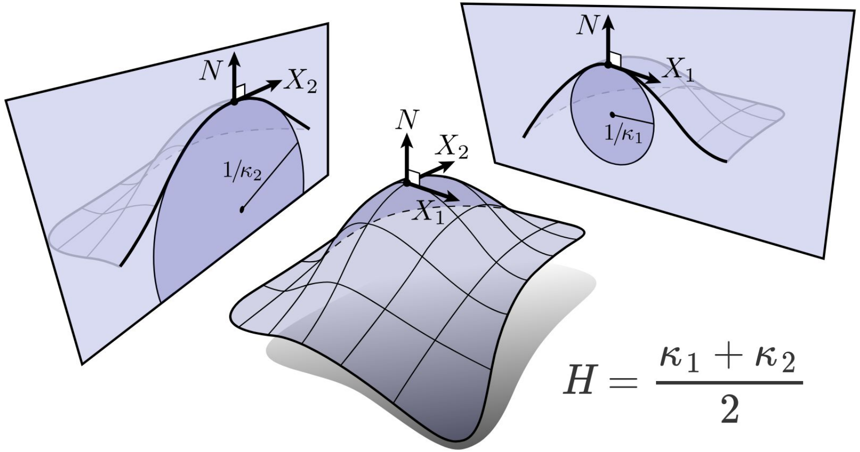


from http://brickisland.net/cs177/?p=144

Biological Membranes: Brief Background

Theory

Differential Geometry (Curvature)



from http://brickisland.net/cs177/?p=144

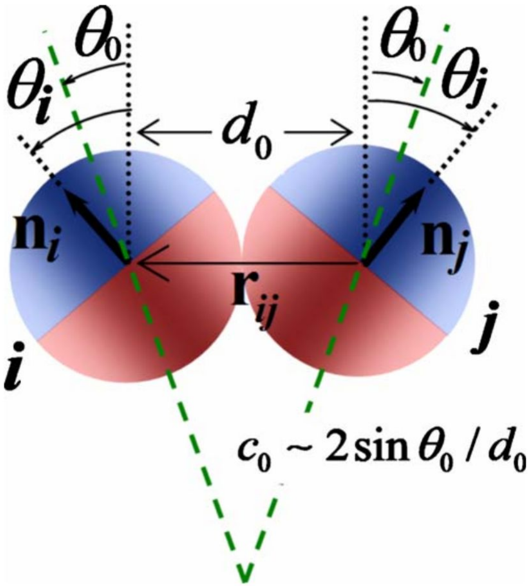
Bending energy: Helfrich (1986)

Bending Rigidity

Spontaneous Curvature

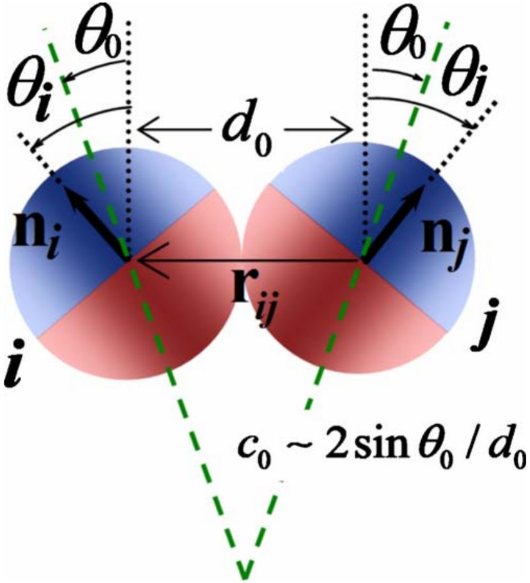
$$E[\boldsymbol{\alpha}] = \int \frac{k_c}{2}[2H(\theta, \phi; \boldsymbol{\alpha}) + c_0]^2 dA$$

Single-Bead Model



from Yuan et. al. (*Physical Review E.* Vol 82, 011905)

Single-Bead Model



from Yuan et. al. (*Physical Review E.* Vol 82, 011905)

$$U(\mathbf{r}_{ij}, \mathbf{n}_i, \mathbf{n}_j) = \begin{cases} u_R(r) + [1 - \phi(\hat{\mathbf{r}}_{ij}, \mathbf{n}_i, \mathbf{n}_j)]\epsilon, & r < r_{\min} \\ u_A(r)\phi(\hat{\mathbf{r}}_{ij}, \mathbf{n}_i, \mathbf{n}_j), & r_{\min} < r < r_c \end{cases}$$

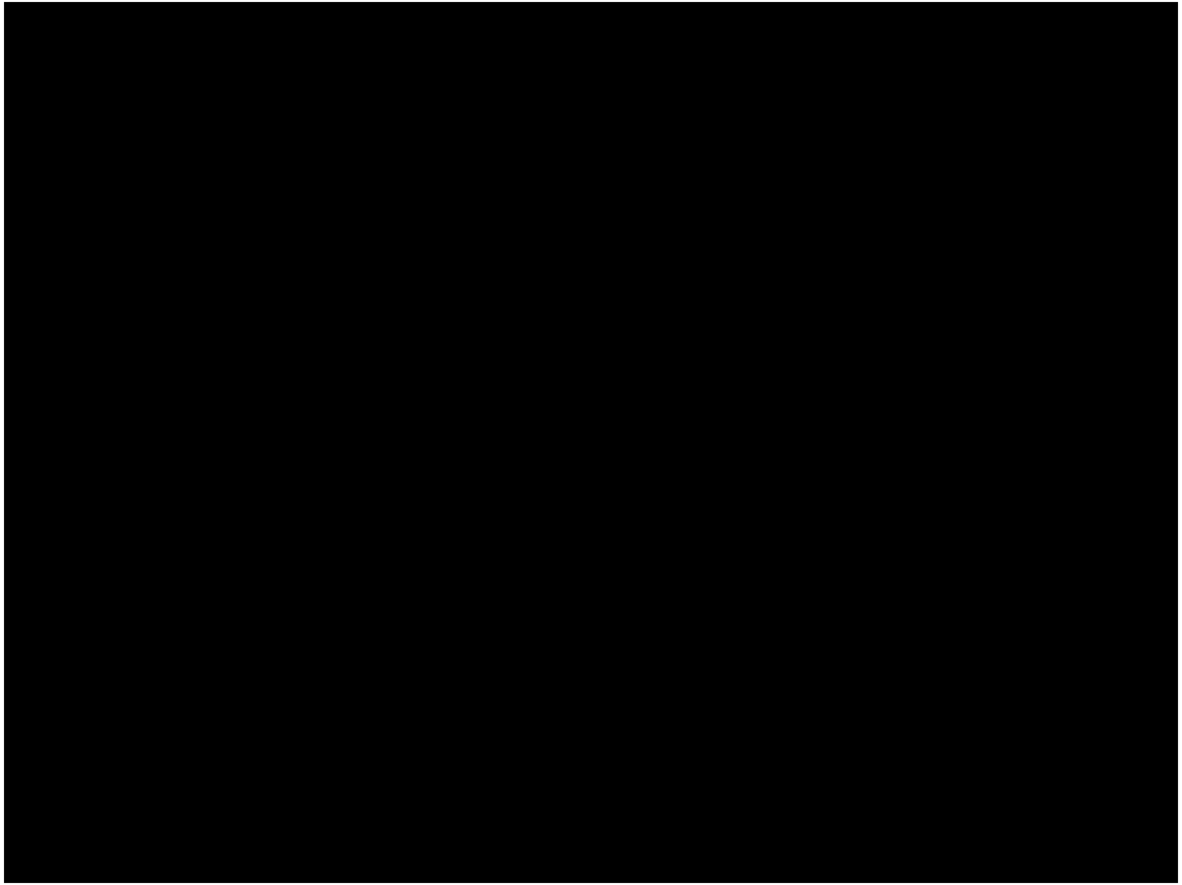
$$u(r) = \begin{cases} u_R(r) = \epsilon\left[\left(\frac{r_{\min}}{r}\right)^4 - 2\left(\frac{r_{\min}}{r}\right)^2\right], & r < r_{\min} \\ u_A(r) = -\epsilon\cos^{2\zeta}\left[\frac{\pi}{2}\frac{(r - r_{\min})}{(r_c - r_{\min})}\right], & r_{\min} < r < r_c \end{cases}$$

$$a = (\mathbf{n}_i \times \hat{\mathbf{r}}_{ij}) \cdot (\mathbf{n}_j \times \hat{\mathbf{r}}_{ij}) + \sin\theta_0(\mathbf{n}_j - \mathbf{n}_i) \cdot \hat{\mathbf{r}}_{ij} - \sin^2\theta_0$$

$$\phi = 1 + \mu[a(\hat{\mathbf{r}}_{ij}, \mathbf{n}_i, \mathbf{n}_j) - 1]$$

Parameters	Interpretations
r_{min}	potential minimum distance
r_c	potential cutoff distance
ζ	steepness of repulsive branch
θ_0	preferred relative orientation
μ	strength of orientation penalty

Our Simulations



Our Simulations

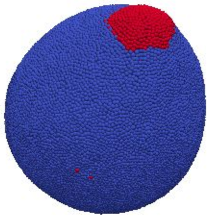
n_{hc} = 0.000

hc: high-curvature

Our Simulations

n_{hc}= 0.000

n_{hc}= 0.025

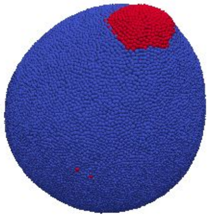


hc: high-curvature

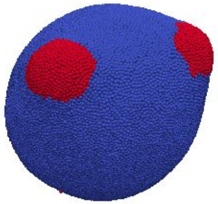
Our Simulations

$n_{hc} = 0.000$

$n_{hc} = 0.025$



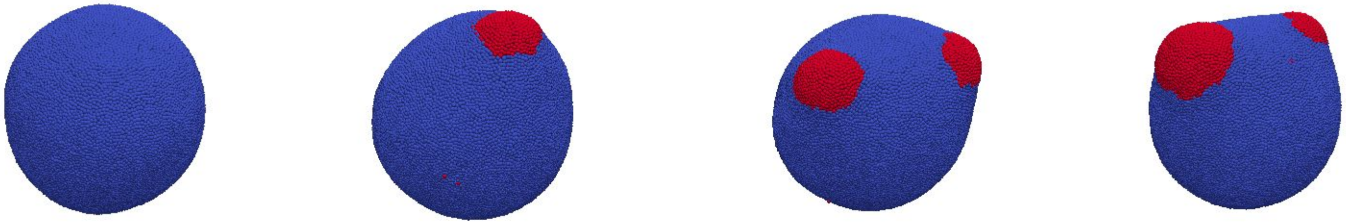
$n_{hc} = 0.050$



hc: high-curvature

Our Simulations

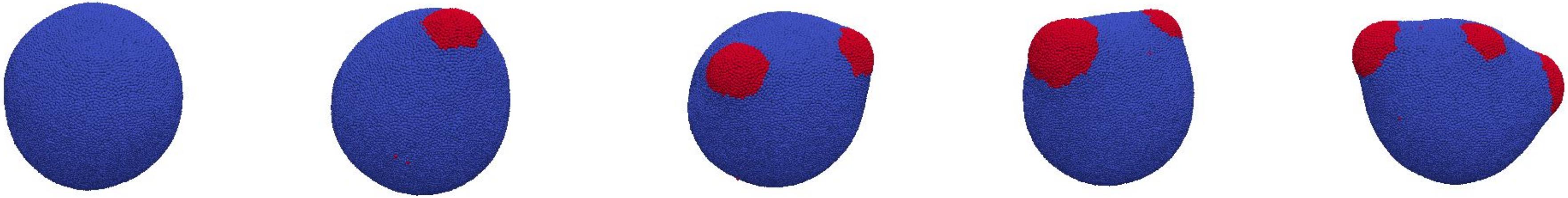
n_{hc} = 0.000 n_{hc} = 0.025 n_{hc} = 0.050 n_{hc} = 0.075



hc: high-curvature

Our Simulations

n_{hc}= 0.000 | n_{hc}= 0.025 | n_{hc}= 0.050 | n_{hc}= 0.075 | n_{hc}= 0.100



hc: high-curvature

Bending Rigidity Estimation

How to quantify shape fluctuations?

- Two-point surface correlation function

Bending Rigidity Estimation

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- Two-point surface correlation function
- Surface autocorrelation function

Bending Rigidity Estimation

How to quantify shape fluctuations?

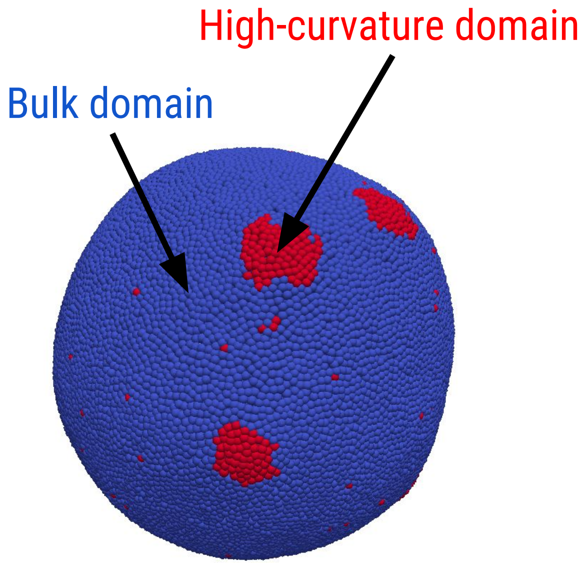
- Two-point surface correlation function
- Surface autocorrelation function
- Fluctuation spectrum of continuum representation

Bending Rigidity Estimation

How to quantify shape fluctuations?

- **Two-point surface correlation function**
- Surface autocorrelation function
- Fluctuation spectrum of continuum representation

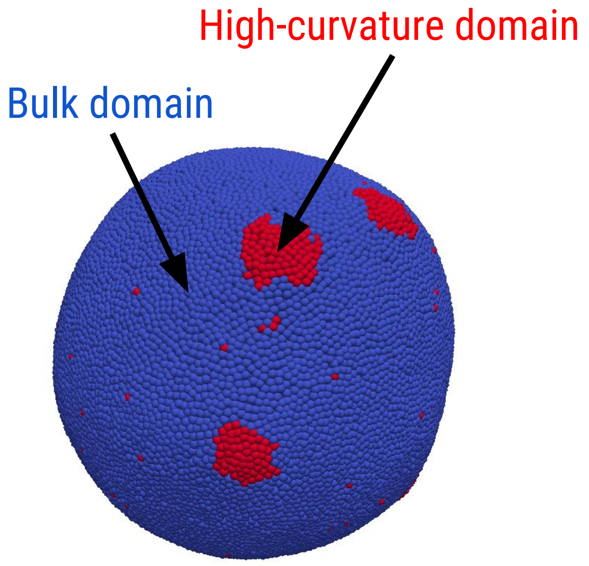
Shape Fluctuations: Two-Point Surface Correlation

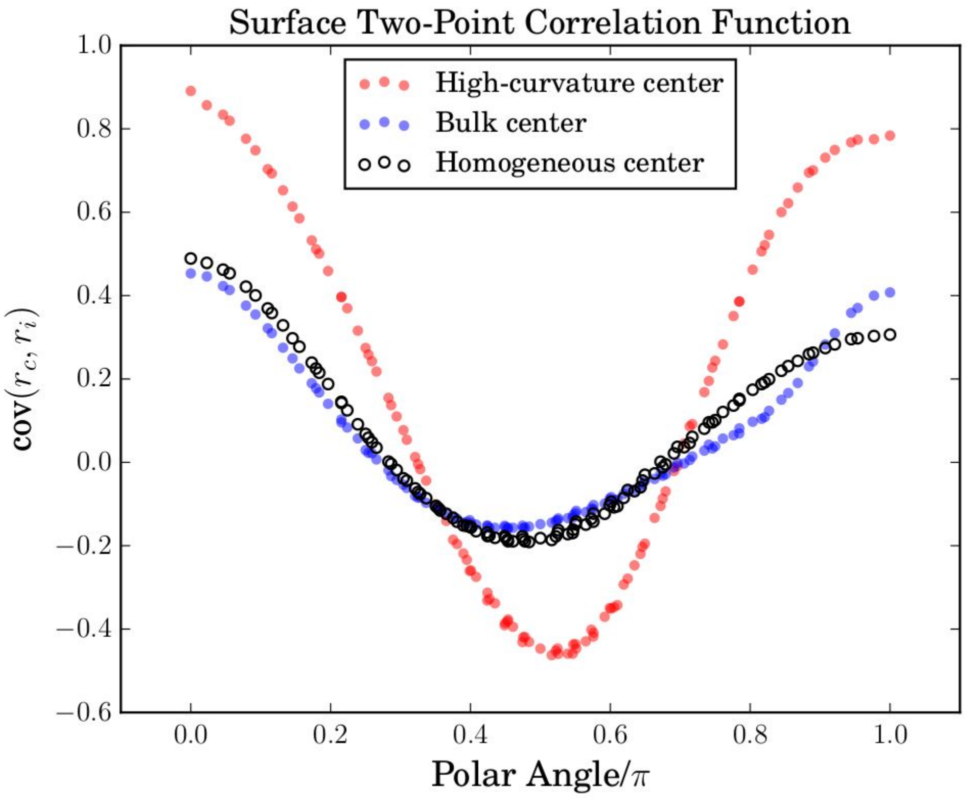


Sampling Procedure

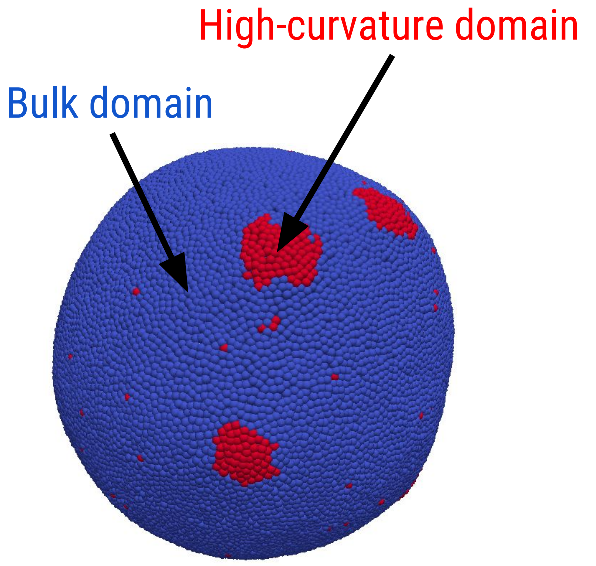
1. Pick random point
2. Rotate point to north pole
3. Random rotation about z-axis
4. Sample correlation function with north pole as center

Shape Fluctuations: Two-Point Surface Correlation

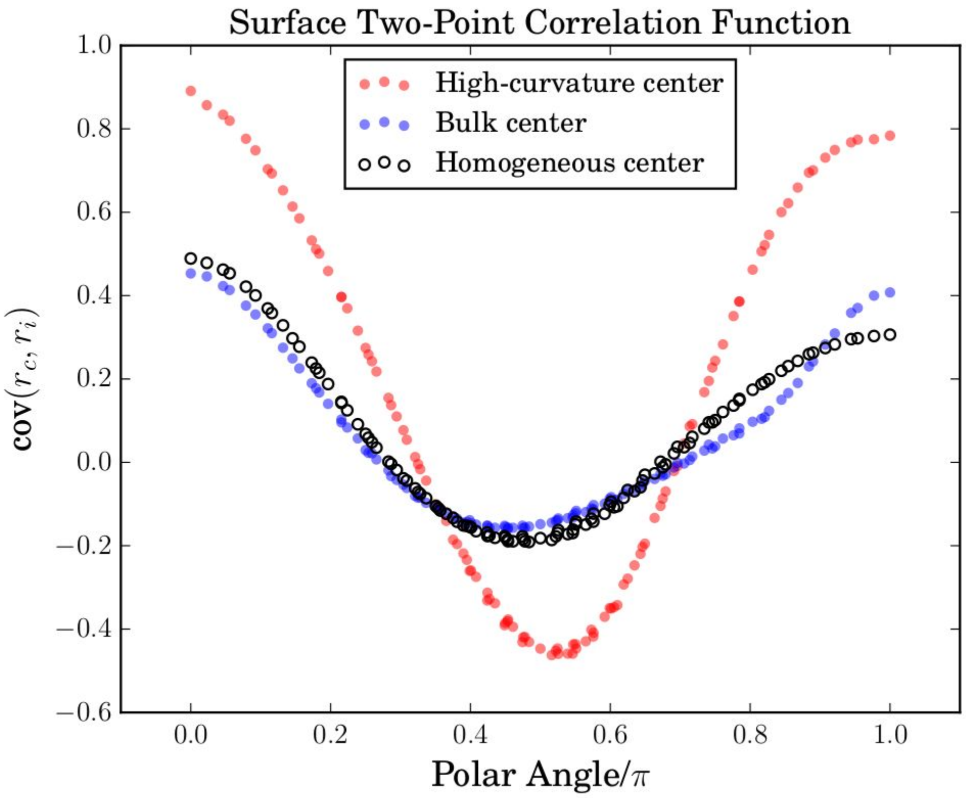




Shape Fluctuations: Two-Point Surface Correlation



More complex shapes cannot be described when homogenizing over rotations...

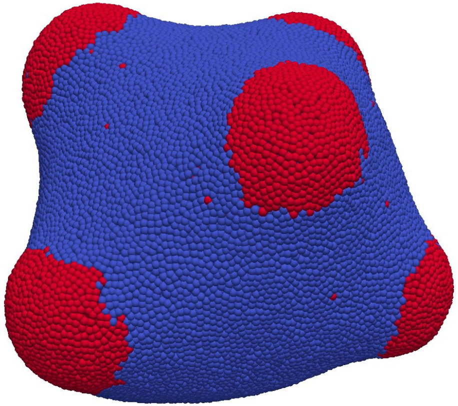


Bending Rigidity Estimation

How to quantify shape fluctuations?

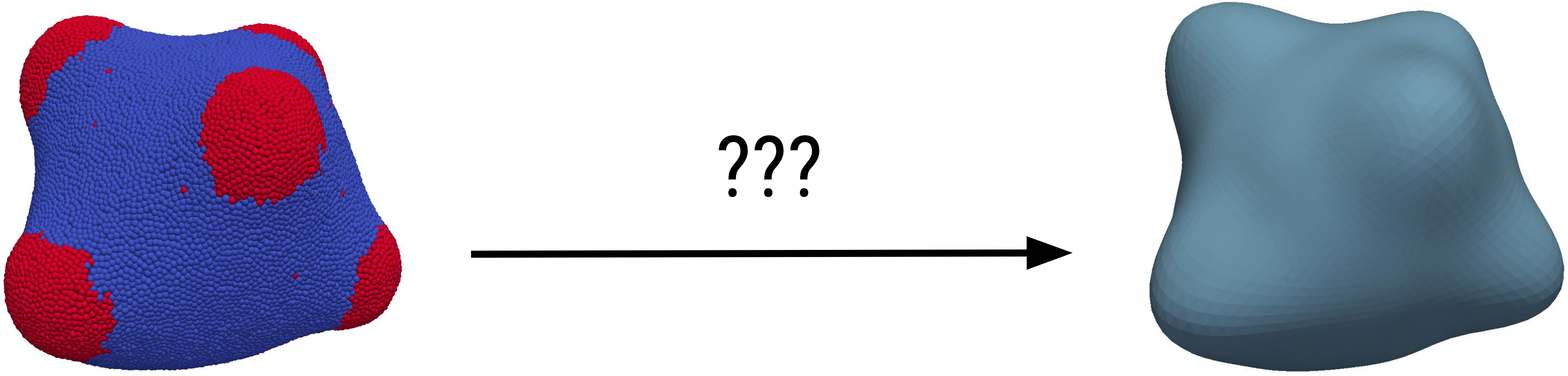
- Two-point surface correlation function
- Surface autocorrelation function
- **Fluctuation spectrum of continuum representation**

Continuum Representation



$$(\mathbf{r}, \boldsymbol{\theta}, \boldsymbol{\phi})$$

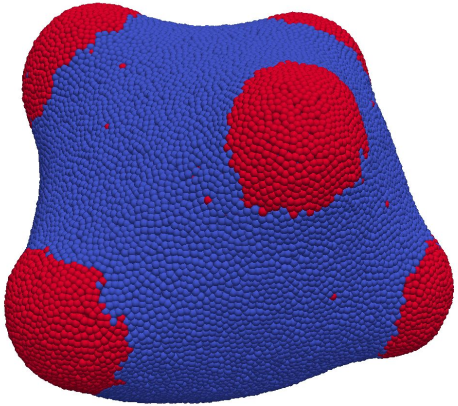
Continuum Representation



$(\mathbf{r}, \boldsymbol{\theta}, \boldsymbol{\phi})$

$r(\theta, \phi; \boldsymbol{\alpha})$

Continuum Representation

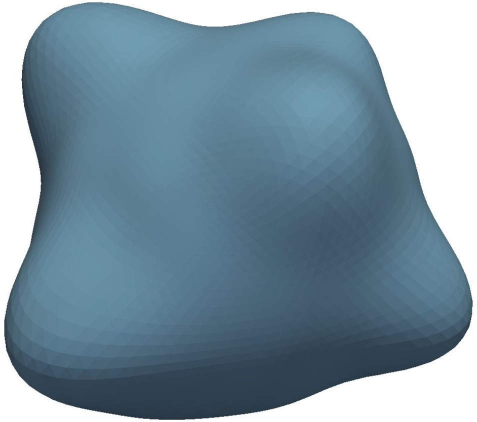


$(\mathbf{r}, \boldsymbol{\theta}, \phi)$

$$r(\theta, \phi) = \sum_i \alpha_i Y^i(\theta, \phi)$$

$$\alpha_i = \int_0^{\pi} \int_0^{2\pi} r(\theta, \phi)(Y^i(\theta, \phi))^* \sin(\theta) d\phi d\theta$$

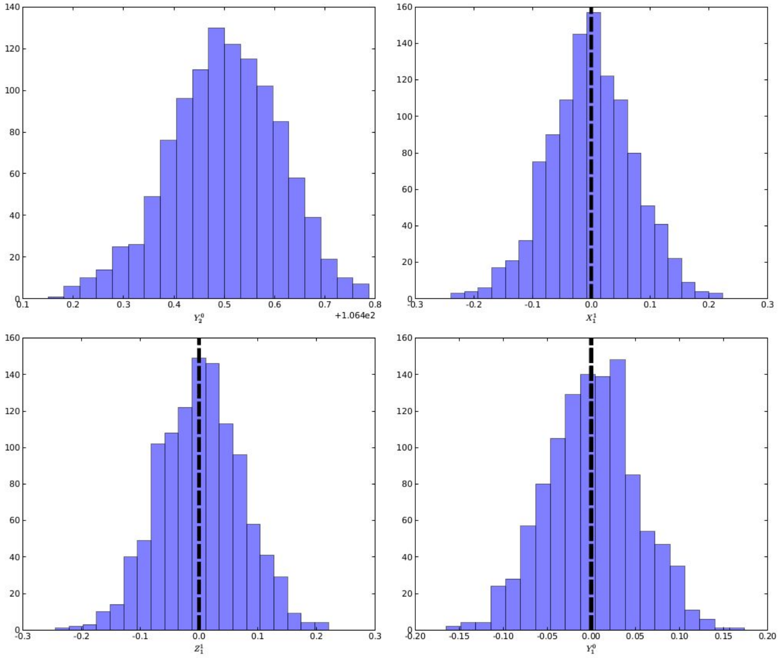
(Evaluated with Lebedev Quadrature)



$r(\theta, \phi; \boldsymbol{\alpha})$

Bending Rigidity Estimation: Mean Shapes

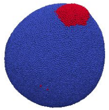
(n_{hc}= 0.000)



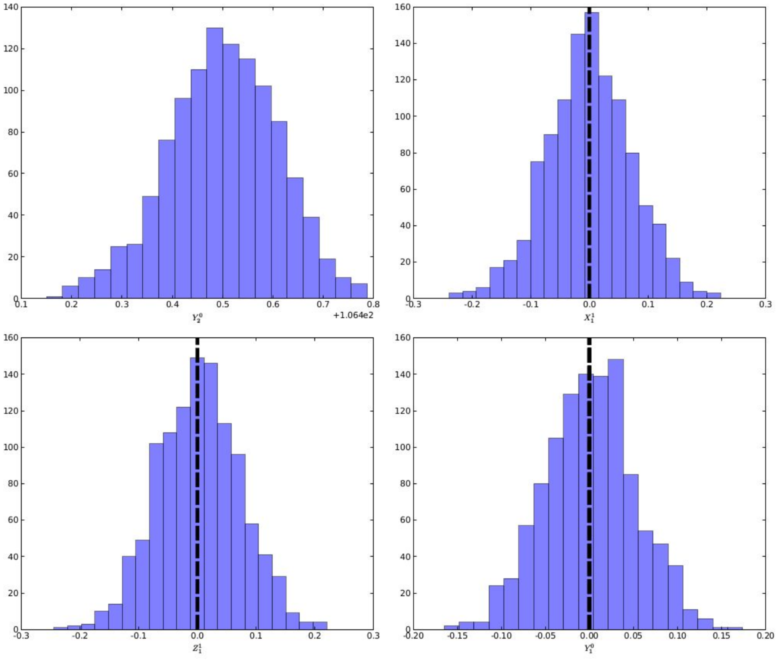
All but l=0 centered around 0

Bending Rigidity Estimation: Mean Shapes

(n_{hc}= 0.000)



(n_{hc}= 0.025)



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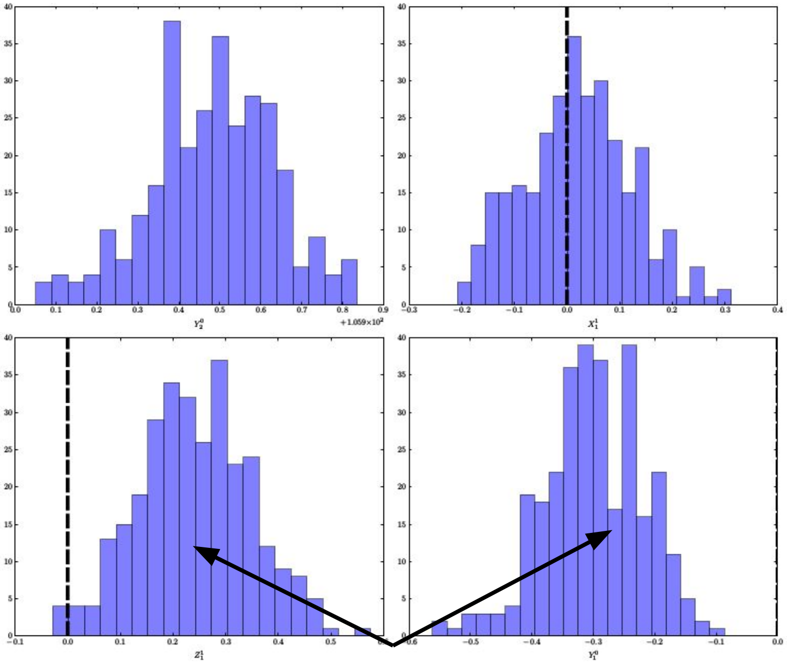

Not centered at 0 anymore!

Bending Rigidity Estimation

Surface:

$$r(\theta, \phi) = \sum_i \alpha_i Y^i(\theta, \phi)$$

Energy Functional:

$$E[\boldsymbol{\alpha}] = \int \frac{k_c}{2}[2H(\theta, \phi; \boldsymbol{\alpha}) + c_0]^2 dA$$

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Expansion about mean shape:

$$E[\boldsymbol{\alpha} + \lambda \mathbf{b}] = E[\boldsymbol{\alpha}] + \lambda(\nabla E\big|_{\boldsymbol{\alpha}})^T \mathbf{b} + \frac{\lambda^2}{2} \mathbf{b}^T \mathrm{Hess}[E]\big|_{\boldsymbol{\alpha}} \mathbf{b} + \mathcal{O}(\lambda^3)$$

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Equilibrium Statistical Mechanics:

$$p(\boldsymbol{\alpha} + \mathbf{b}) \propto \exp\left[-\beta E[\boldsymbol{\alpha} + \mathbf{b}]\right]$$

Bending Rigidity Estimation

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$$p(\boldsymbol{\alpha} + \mathbf{b}) \propto \exp\left[-\beta E[\boldsymbol{\alpha} + \mathbf{b}]\right] \propto \exp\left[-\frac{1}{2} \mathbf{b}^T \mathrm{C}^{-1} \mathbf{b}\right]$$

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where $\mathrm{C}^{-1} \equiv \beta k_c \mathrm{Hess}\left[\int [2H(\theta,\phi;\boldsymbol{\alpha}) + c_0]^2 dA\right]\Big|_{\boldsymbol{\alpha}}$

Bending Rigidity Estimation

Equilibrium Statistical Mechanics:

$$\mathrm{C}^{-1} \equiv \beta k_c \mathrm{Hess}\left[\int [2H(\theta,\phi;\boldsymbol{\alpha}) + c_0]^2 dA\right]\Big|_{\boldsymbol{\alpha}}$$

Analytic expression?

Bending Rigidity Estimation

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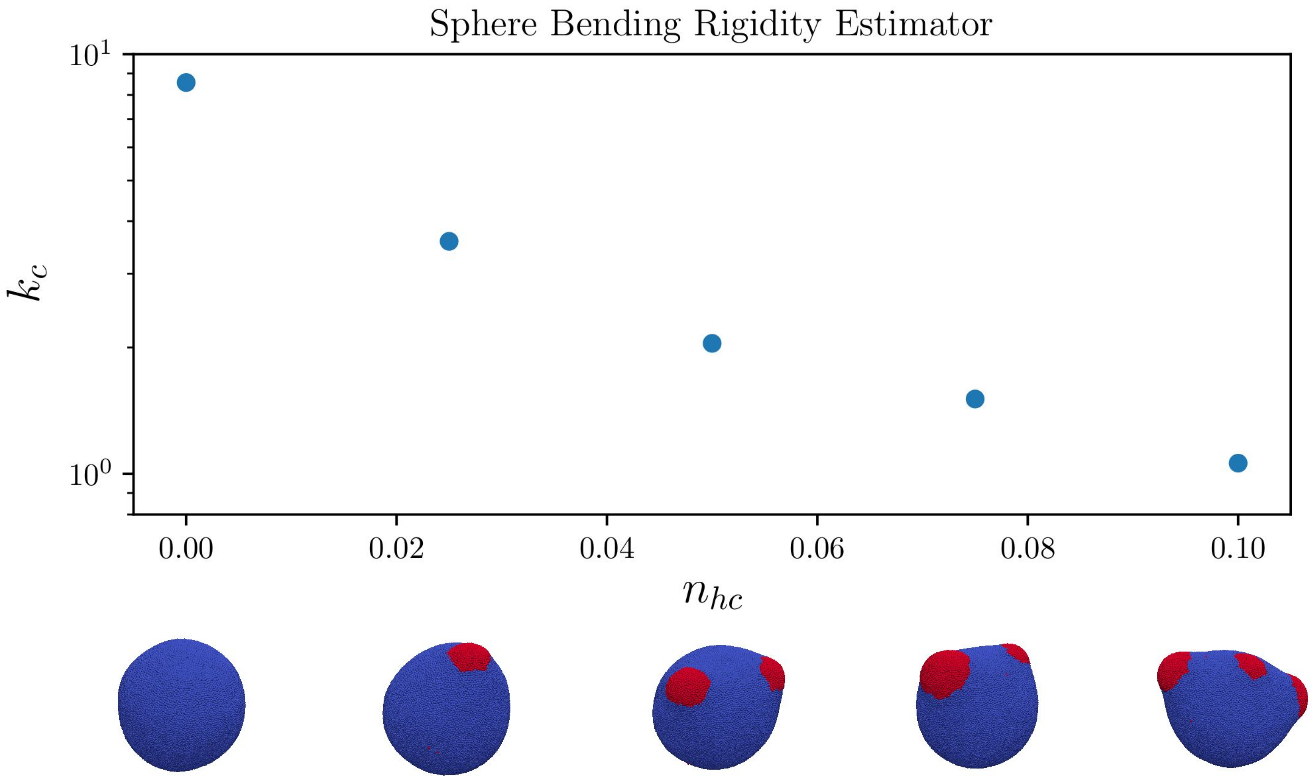
Analytic expression?

$$c_0 = -2r_0^{-1}$$

$$\delta^2 E = \frac{k_c}{2r_0^2}\sum_{l,m}|a_{lm}|^2(l^2(l+1)^2 - 4)$$

Bending Rigidity Estimation: Results



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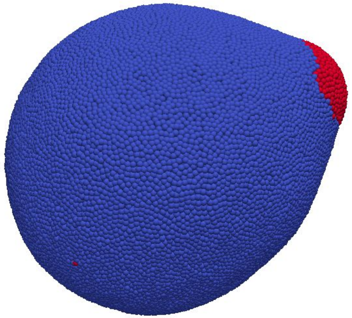

$$c_0 = -2H(\theta,\phi;\boldsymbol{\alpha}_0)$$

$\delta^2 E =$???

Bending Rigidity Estimation

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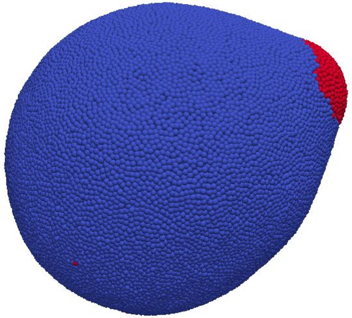
Our Estimation:

1) Calculate matrix from theory
    1) Mean curvature: Sympy



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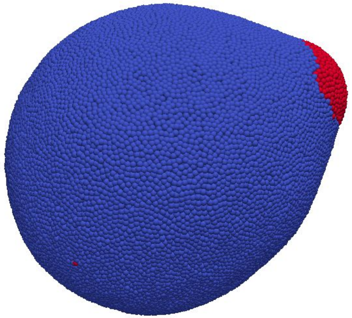
    1) Mean curvature: Sympy
    2) Integral: Lebedev quadrature



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1) Calculate matrix from theory
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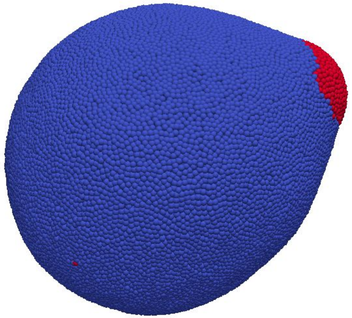
   2) Integral: Lebedev quadrature
   3) Hessian: central differencing



$$c_0 = -2H(\theta,\phi;\boldsymbol{\alpha}_0)$$

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Bending Rigidity Estimation

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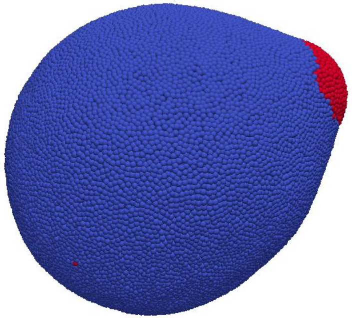
$$\delta^2 E = \frac{k_c}{2r_0^2}\sum_{l,m}|a_{lm}|^2(l^2(l+1)^2 - 4)$$



$$c_0 = -2H(\theta,\phi;\boldsymbol{\alpha}_0)$$

$\delta^2 E =$???

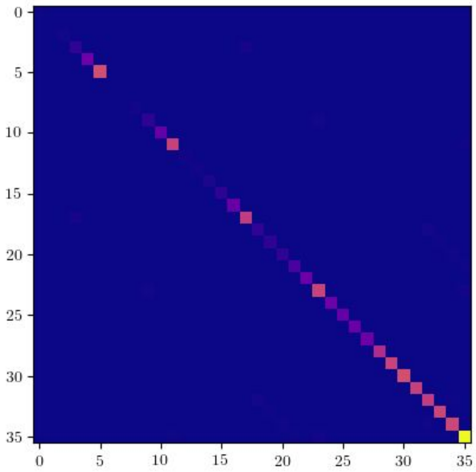
Our Estimation:

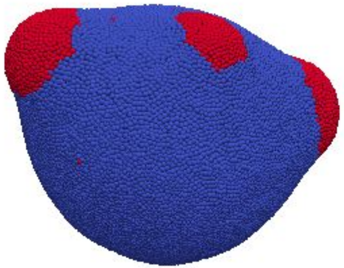
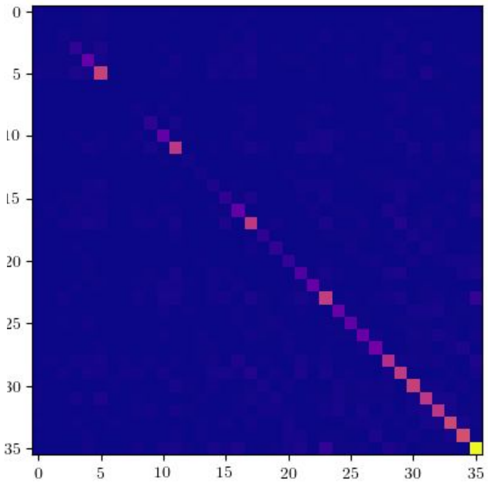
1) Calculate matrix from theory
   1) Mean curvature: Sympy
   2) Integral: Lebedev quadrature
   3) Hessian: central differencing
2) Compare with $\mathrm{cov}(\mathbf{b},\mathbf{b})$ from simulations

Bending Rigidity Estimation

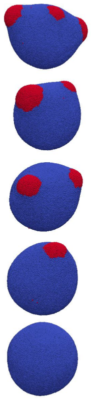
Equilibrium Statistical Mechanics:

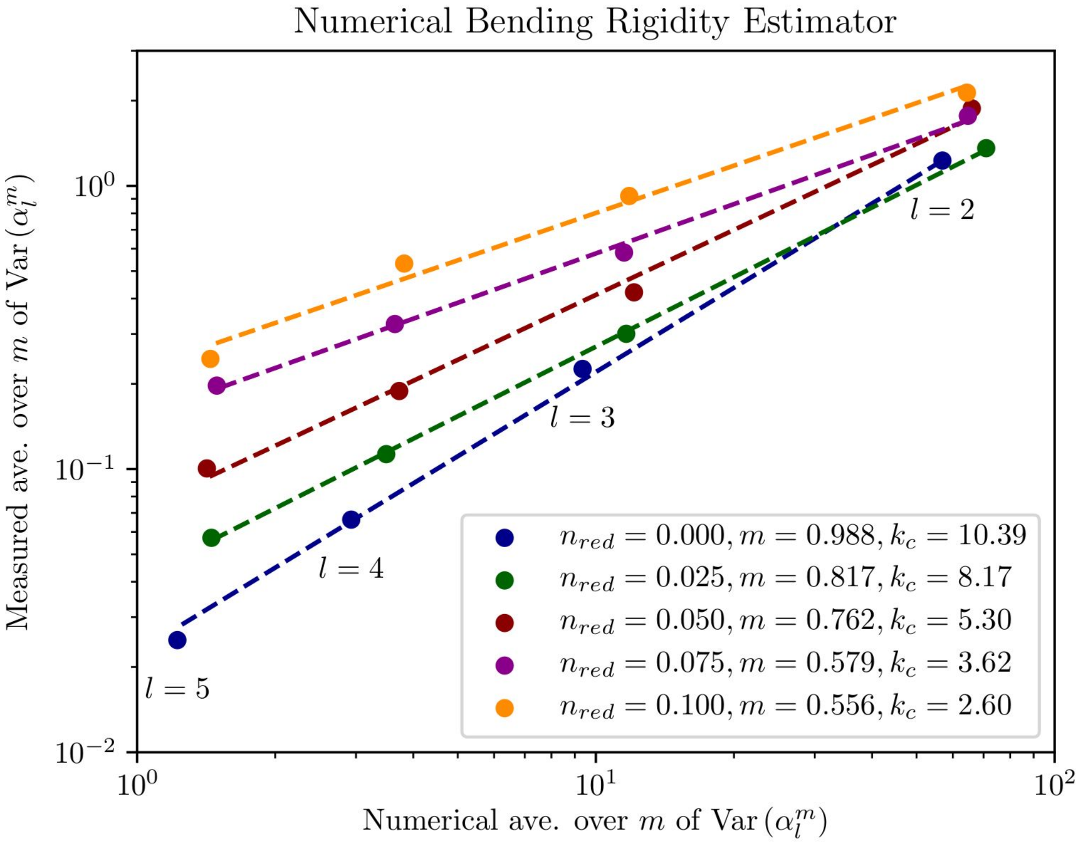
$$C^{-1} \equiv \beta k_c \mathrm{Hess}\left[\int [2H(\theta,\phi;\boldsymbol{\alpha}) + c_0]^2 dA\right]\Big|_{\boldsymbol{\alpha}}$$

Bending Rigidity Estimation: Results





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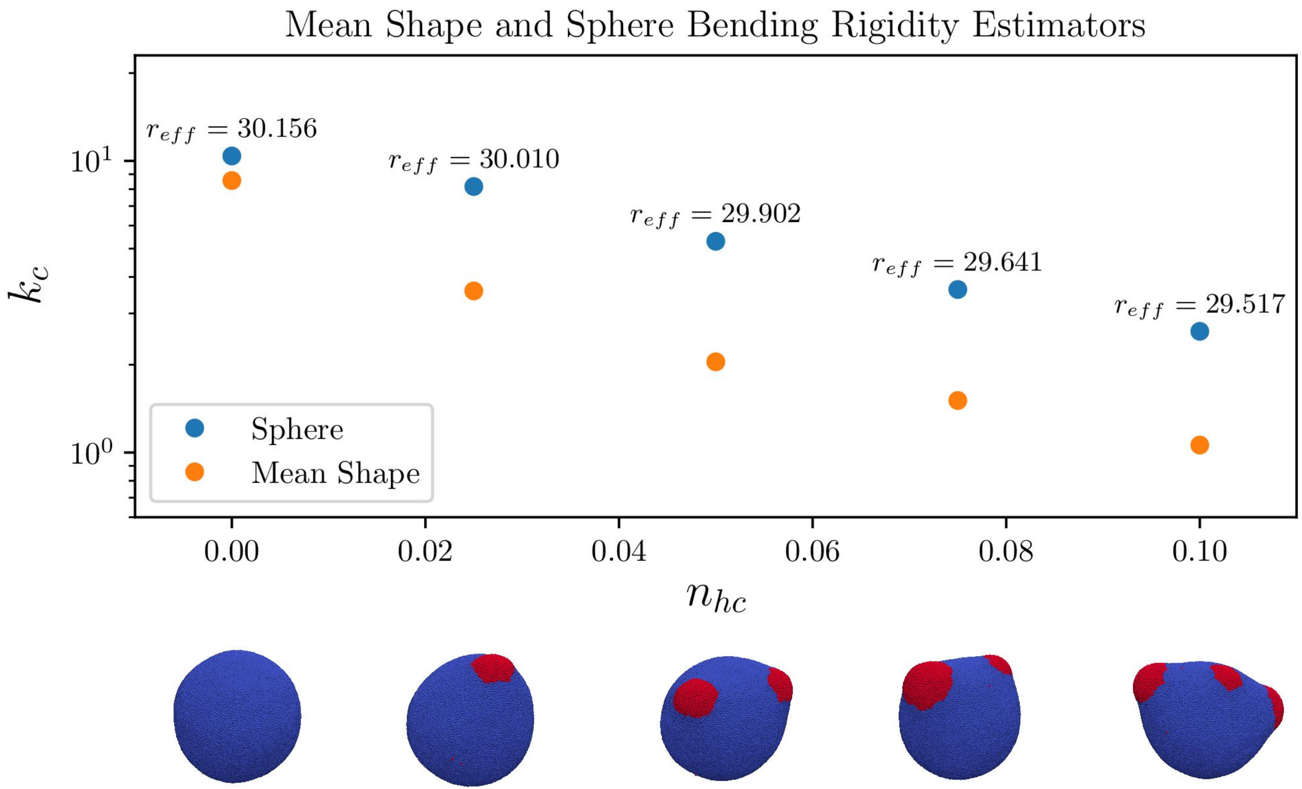
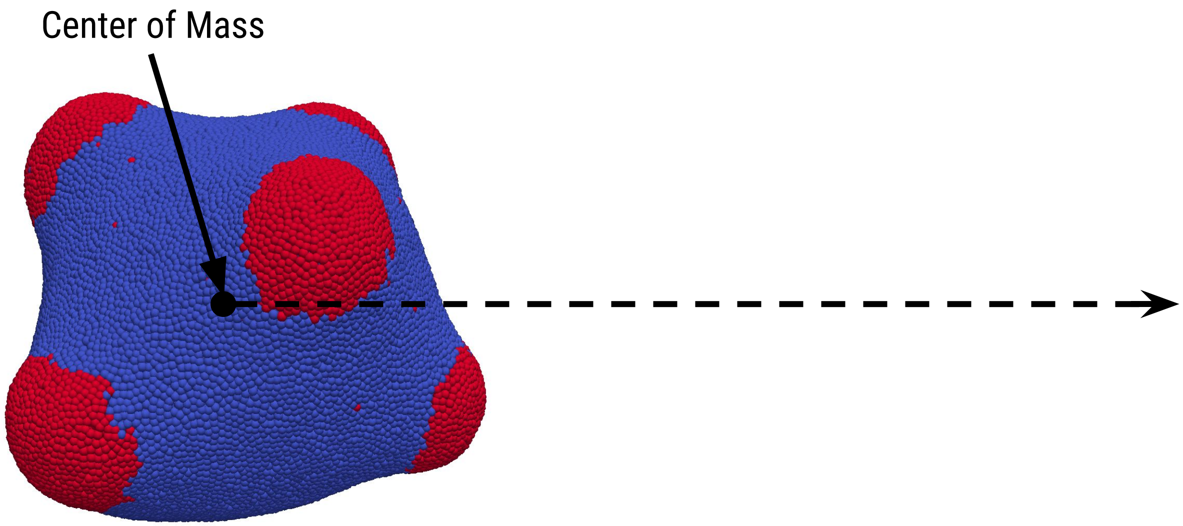


Shape Fluctuations: “Plane Distance”



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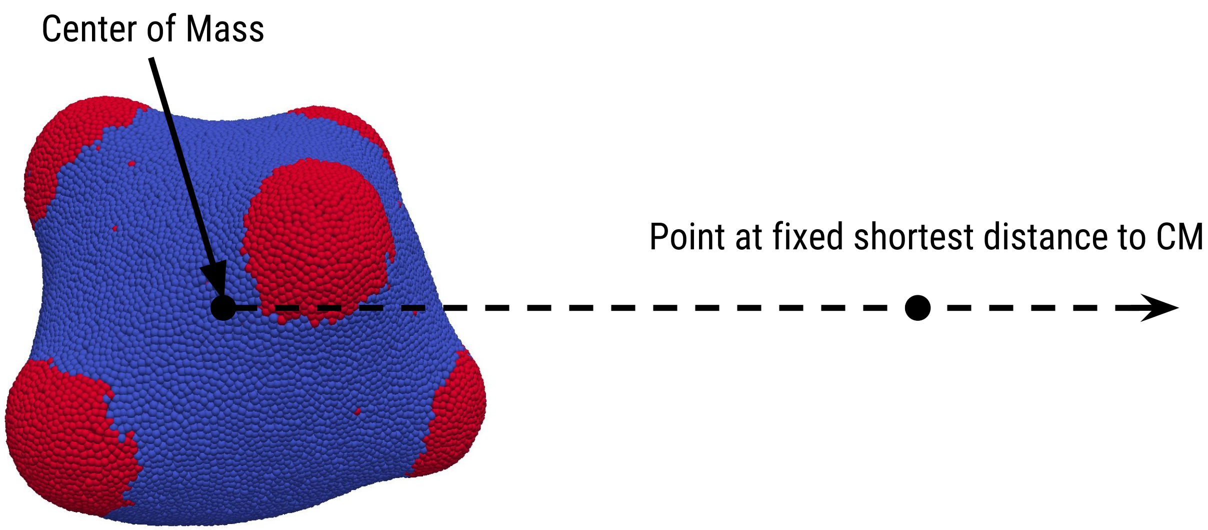

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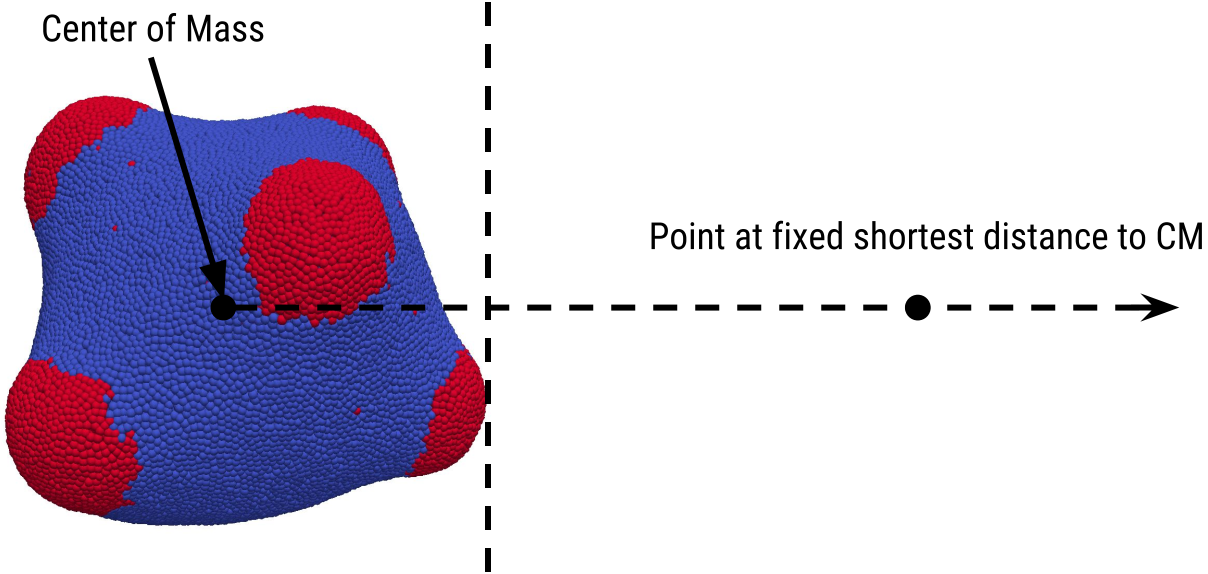

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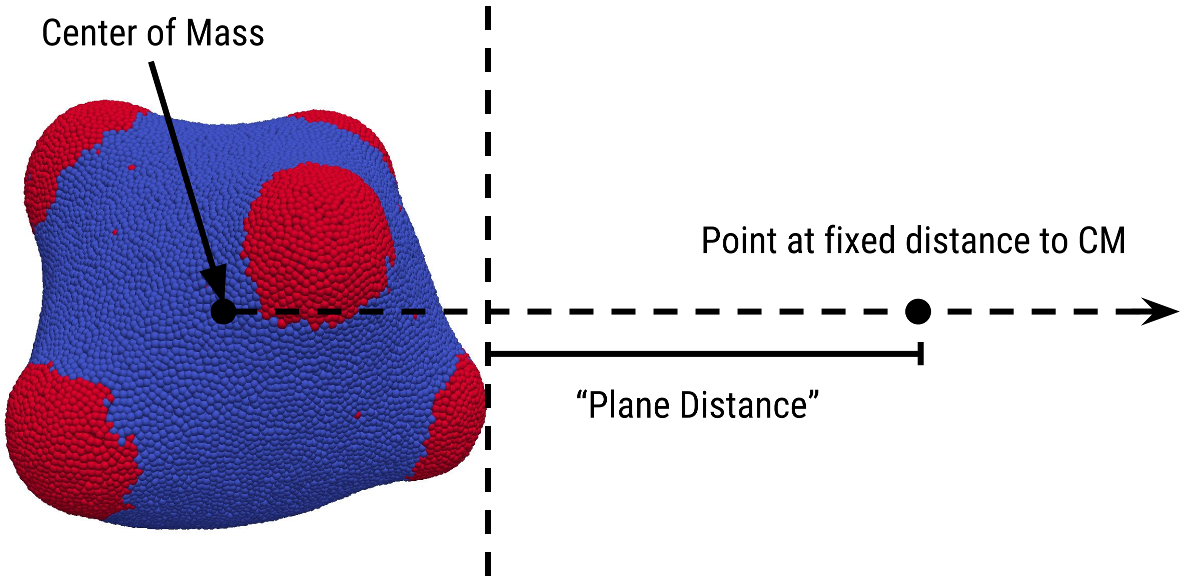

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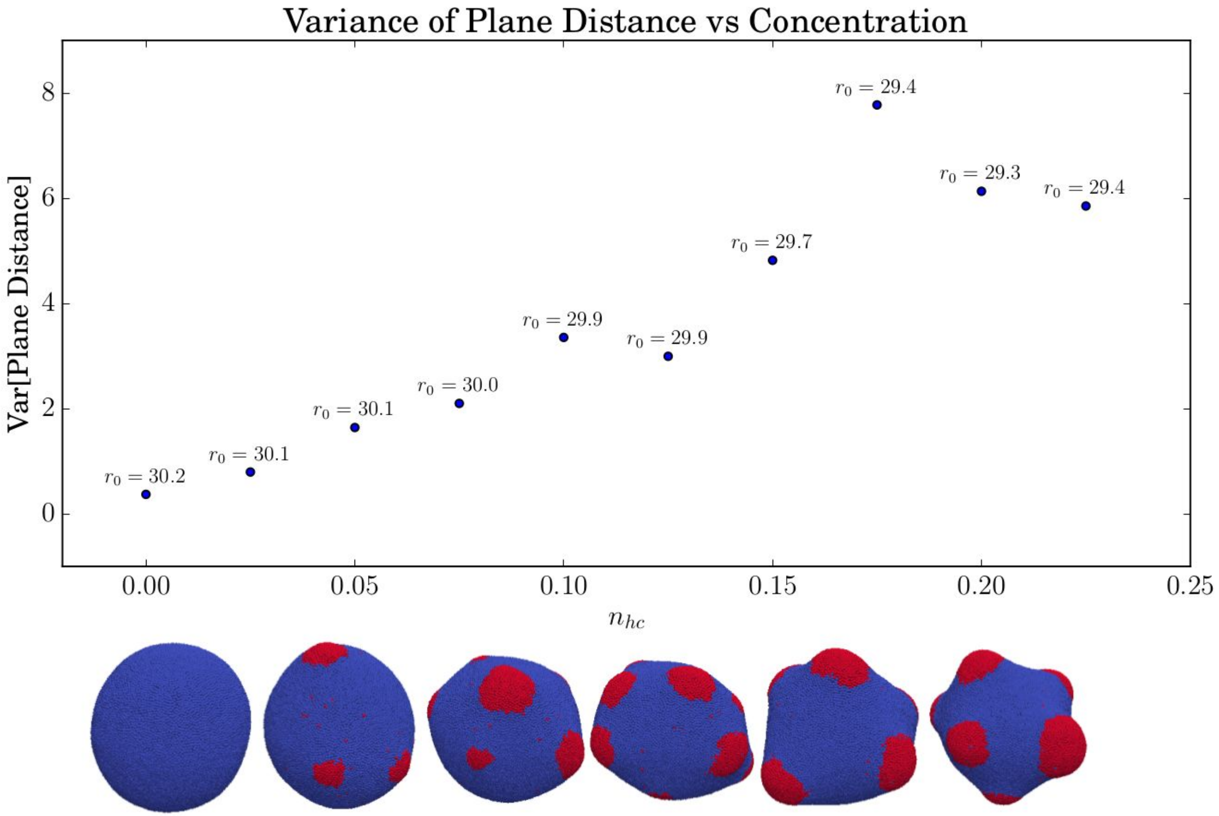

More high curvature domains

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Higher variance in plane distance

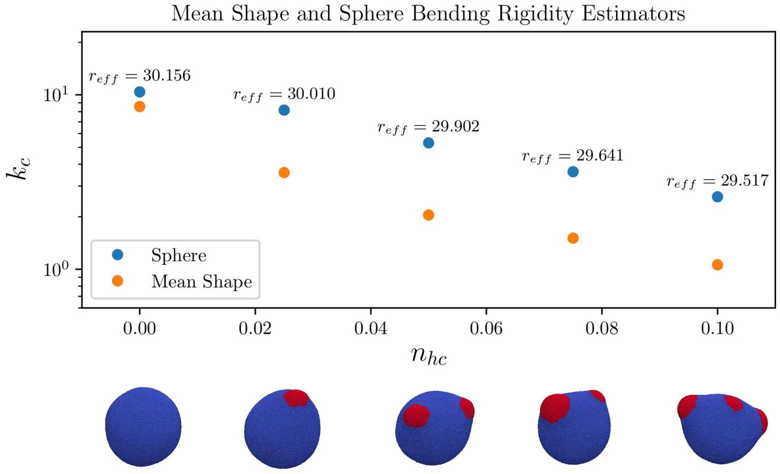
Summary

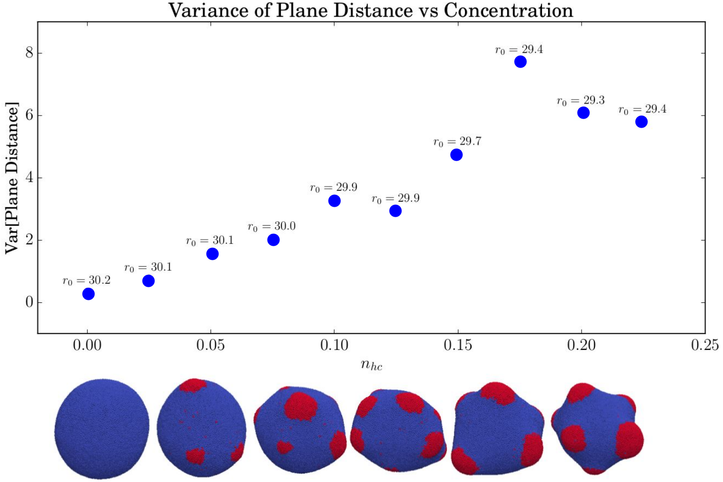
Domains form from embedded high-curvature species.

Using naive theory for bending-rigidity estimation is a decent start

- Gives right monotonic relationship
- Linearized theory falls apart as shape becomes more irregular

Heterogeneities influencing geometry may be a key component in adhesion dynamics.





Next Steps

Develop more efficient/robust numerical methods for Hessian.

Explore effects of much higher heterogenieties on bending rigidity.

Explore effects of fluctuating hydrodynamics (coupling between coarse-grained beads and continuum stochastic fields representing solvent).

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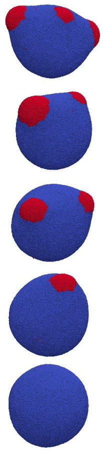
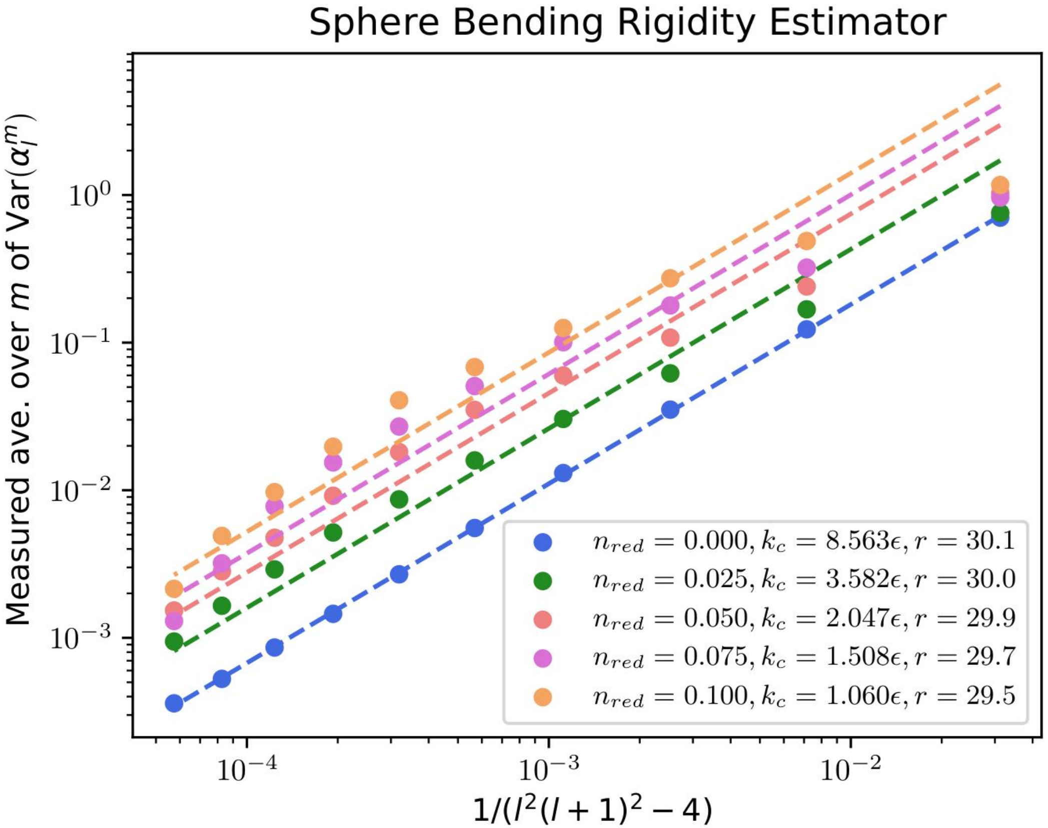
Backup Slides

Bending Rigidity Estimation: Results





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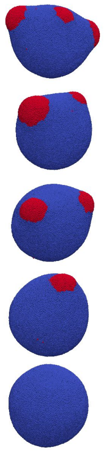

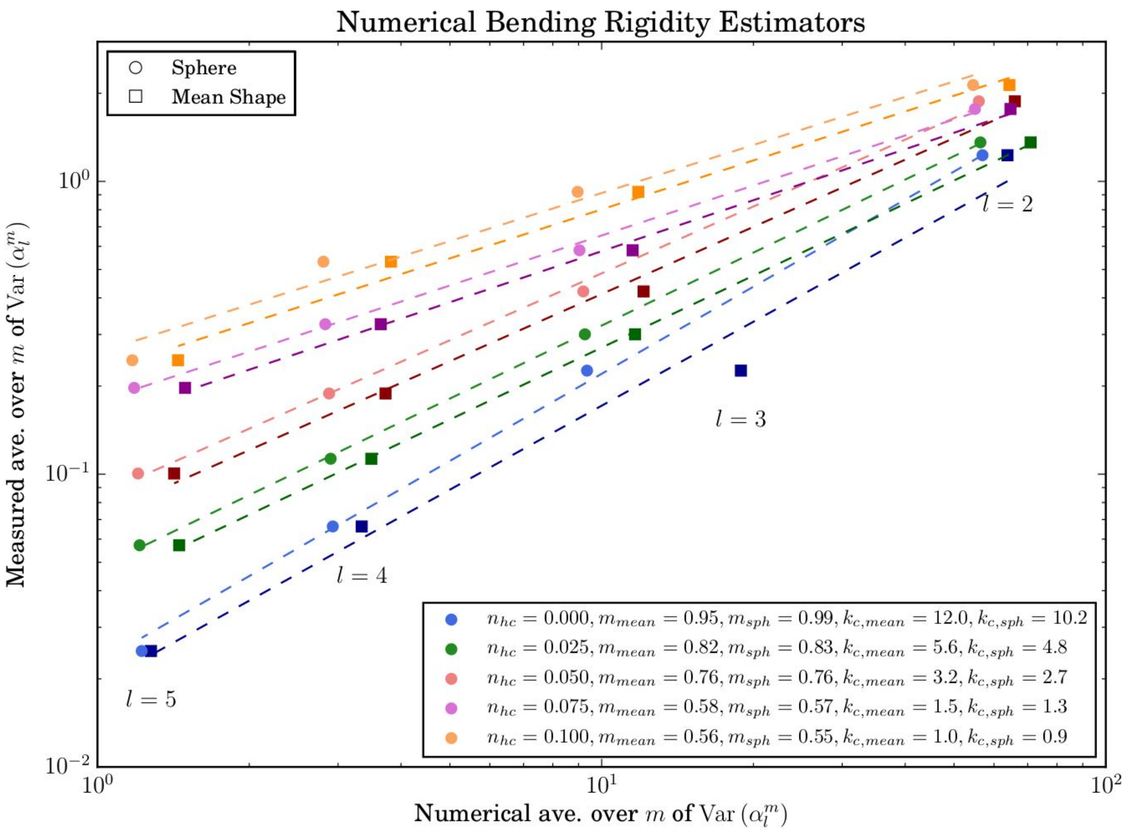

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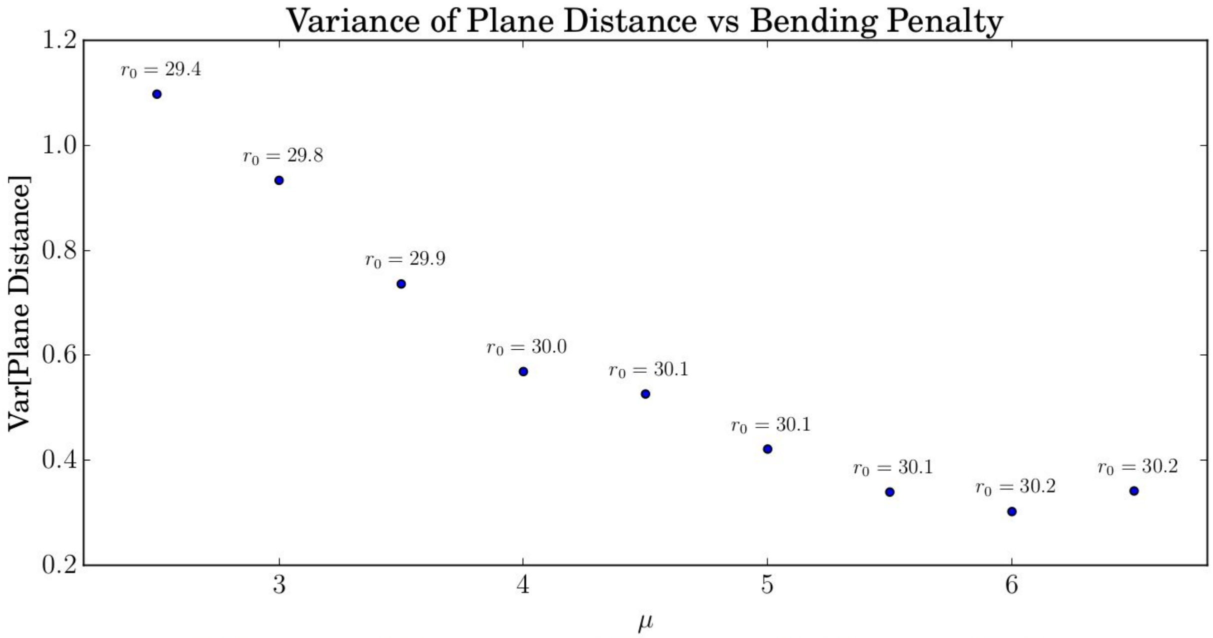

Stiffer Homogeneous Vesicle

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Lower variance in plane distance